Universität Basel

Research Project

Drosophila Branching 2.0

Third-party funded project

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How animals acquire their distinct and species-specific shapes and three-dimensional morphologies and how such morphologies are encoded in the genome has been a fascinating topic for numerous scientists over many decades. While the question of how animal form and diversity is achieved is fascinating, gaining a cellular and molecular understanding of the phenomenon of morphogenesis requires breaking down the problem into more precise or better defined questions, such as how individual parts of an animal, for example external extremities or internal organs reach their precise shape during development.My laboratory has tried to answer questions related to the overall topic of animal morphogenesis by using genetic approaches, mainly in Drosophila melanogaster, the fruit fly, and more recently also in Danio rerio, the zebrafish. In this grant application, we would like to capitalise on recent developments in our lab and answer two sets of questions that have preoccupied us over a long period. We and others have studied tracheal development in drosophila as a paradigm for a complex morphogenesis process. We have shown that cell rearrangements are key to generate the distinct morphologies of different tracheal branches in the drosophila tracheal system, and that these cell rearrangements are controlled by transcription factors such as Spalt and Knirps and by cellular activities such as cell migration, cell shape changes and adherens junction remodelling. However, we know very little about the targets of these transcriptional regulators and their cellular and molecular functions in regulating cell rearrangements. We propose to undertake transcriptional profiling to unravel the key role of the Spalt transcription factor. Profiting from the efficiency of Crispr-based methods in drosophila and the short generation time, functional studies of candidate genes can then rapidly be performed and the data integrated into the existing molecular networks. While we hope to isolate more genes involved in the control of cell rearrangement starting from transcriptional profiling, it is very likely that many genes or proteins involved in tracheal morphogenesis have not been identified using classical zygotic loss of function mutagenesis, due to maternal contribution. We have recently developed a nanobody-based method allowing for the depletion of maternally provided proteins in specific tissues and study their role in morphogenesis processes. Using this novel approach, we would like to undertake a pioneering pilot screen to search for proteins with hitherto uncharacterized roles in the tracheal system and in the amnioserosa, a central force-producer during the tissue morphogenesis process of dorsal closure. Furthermore, and inspired by the wealth of nanobody-based novel tools we have already designed and used in drosophila, we want to introduce and validate novel protein-directed approaches based on short peptide tags and the corresponding binding proteins reported to be functional in cultured cells. If these tools work well in multicellular organisms where they have not been tested yet, a wealth of novel applications in developmental biology will emerge, which will help us studying candidate genes from our screens.Question 1: How is the process of cell intercalation regulated at the molecular level?Aim 1: Identify Spalt-regulated genes using RNAseq and

study their role in cell intercalationQuestion 2: Can we identify many more proteins involved in tracheal branching morphogenesis, whose contribution has not yet been identified? Aim 2: Identify novel genes (proteins) regulating tracheal morphogenesis using deGradFP.Question 3: Can short peptides be used for in vivo tagging and subsequent protein manipulation?Aim 3: Generate/validate novel tools to directly study proteins in morphogenesis processes

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